

Syntheses of Many-membered Rings. Part 28† Kinetic Models for the Irreversible Cyclisation of Two Symmetrical Monomers

Gianfranco Ercolani,* Luigi Mandolini,* and Paolo Mencarelli*

Centro C.N.R. di Studio sui Meccanismi di Reazione and Dipartimento di Chimica, Università 'La Sapienza,' 00185 Roma, Italy

The reaction of two symmetrical bifunctional reactants A–A and B–B to give monomeric rings (two-component ring closure) has been simulated by means of two complementary kinetic models. These provide underestimated and overestimated values, respectively, of the yields of ring product as a function of both the initial concentration of monomers in batch processes and their rate of feed into the reaction medium in influxion processes (Ziegler high dilution conditions). The merits and limitations of the two models are discussed. Comparison with analogous results previously reported for the reaction of unsymmetrical bifunctional reactants A–B (one component ring-closure) shows that more stringent dilution requirements are to be met by the two-component reaction system. The merging of the influxion conditions into the batch-wise ones has also been investigated. It is shown that this occurs on increasing the feed rate beyond a certain critical value. Above this value the system can seemingly display an intriguing insensitivity to dilution.

Macrocycles are usually prepared either by ring closure of unsymmetrical bifunctional chains of the type A–B, or, in most cases, by reaction of two symmetrical monomers of the type A–A and B–B.² In both cases the competitive polymerisation process limits the yield of the ring being formed, thus making the outcome of a macrocyclisation procedure hardly predictable without resorting to kinetic models in which simultaneous cyclisation and polymerisation are taken into account. The tremendous complexity of the general problem imposes simplifying approximations,³ but the requirement for the results of the calculations to be widely applicable to real systems severely limits the kind and number of approximations allowed.

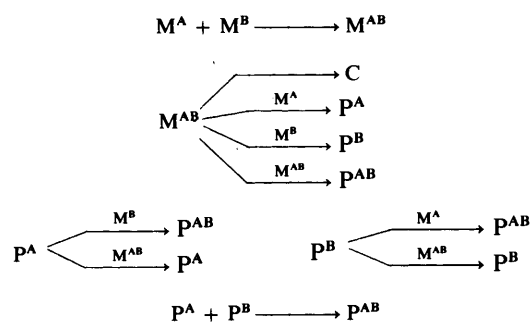
In previous papers we have thoroughly investigated the problems connected with the kinetic treatment of the irreversible reaction of a reactant of the type A–B.^{3–5} Our efforts culminated with the development of a computer program (CYCLES) able to predict the distribution of cyclic products at various levels of approximation.⁴

As a first step in the inclusion in the CYCLES program of the two-component ring closure A–A + B–B, carried out both under batch-wise and influxion conditions, we report here two complementary kinetic models, which describe the reacting system at the lowest level of approximation in that only the formation of the monomeric ring is explicitly taken into account. The merits and limitations of the two models are presented and discussed.

Kinetic Treatment and Results

The Overestimating Model (OM).—In the following treatment it will be assumed that A and B are two different functional groups each capable of reacting irreversibly only with the other, and whose inherent reactivity (k_{inter}) is independent of the size of the molecule to which they are attached.⁶ Here k_{inter} may be defined with reference to a model reaction between monofunctional reactants, namely, –A + B–, where the nature of the residues attached to the A and B functionalities resemble as closely as possible that of the chains connecting the end groups in A–A and B–B, respectively. It will be also assumed that the system is homogeneous throughout the entire course of the reaction.

Let us consider the simplified kinetic model outlined in



Scheme 1.

Scheme 1, where M^A , M^B , and M^{AB} represent the acyclic monomers A–A, B–B, and A–AB–B; P^A , P^B , and P^{AB} , the acyclic polymers A–(AB–BA–)_{n–1} A, B–(BA–AB–)_{n–1} B and A–A(B–BA–A)_{n–1} B–B, with $n > 1$; and C, the cyclic monomer. In Scheme 1 the polymer P^{AB} has no influence on the reaction course, thus implying that P^{AB} may be viewed as being either unreactive or capable of undergoing only intramolecular reactions. This is equivalent to saying that the effective molarities (*vide infra*) of the polymeric rings are infinitely large. As a consequence, Scheme 1 overestimates the yield of C, in that it does not take into account the amounts of M^A , M^B , and M^{AB} diverted into polymeric products by reaction with P^{AB} . For this very reason we indicate the kinetic model outlined in Scheme 1 as being the *overestimating model*.

The set of rate equations relative to the OM can be formulated as follows:

$$d[M^A]/dt = -2k_{inter}[M^A](2[M^B] + [M^{AB}] + 2[P^B]) \quad (1)$$

$$d[M^B]/dt = -2k_{inter}[M^B](2[M^A] + [M^{AB}] + 2[P^A]) \quad (2)$$

$$d[M^{AB}]/dt = 4k_{inter}[M^A][M^B] - k_{intra}[M^{AB}] - 2k_{inter}[M^{AB}](2[M^A] + [M^B] + [M^{AB}] + [P^A] + [P^B]) \quad (3)$$

$$d[C]/dt = k_{intra}[M^{AB}] \quad (4)$$

† For Part 27, see ref. 1.

$$d[P^A]/dt = 2k_{\text{inter}}[M^A][M^{AB}] - 4k_{\text{inter}}[P^A]([M^B] + [P^B]) \quad (5)$$

$$d[P^B]/dt = 2k_{\text{inter}}[M^B][M^{AB}] - 4k_{\text{inter}}[P^B]([M^A] + [P^A]) \quad (6)$$

where k_{intra} is the specific rate for cyclisation of M^{AB} . Derivation of the statistical factors appearing in the rate equations is straightforward, apart from those related to the dimerisation of M^{AB} which deserve a comment. Indeed, one must pay attention to the fact that two molecules of M^{AB} disappear upon dimerisation and that the specific rate for dimerisation is simply k_{inter} .³

Since the critical parameter to characterise intramolecular reactions is the effective molarity (EM), defined as the ratio $k_{\text{intra}}/k_{\text{inter}}$,^{7,8} it is convenient to divide equations (1)–(6) by a dimensionless constant f of the same numerical value as k_{inter} . This operation changes the time scale ($t' = ft$) and makes the terms k_{intra} and k_{inter} numerically equal to EM and 1 respectively. The set of equations (1)–(6) therefore simplifies to equations (7)–(12).

$$d[M^A]/dt' = -2[M^A](2[M^B] + [M^{AB}] + 2[P^B]) \quad (7)$$

$$d[M^B]/dt' = -2[M^B](2[M^A] + [M^{AB}] + 2[P^A]) \quad (8)$$

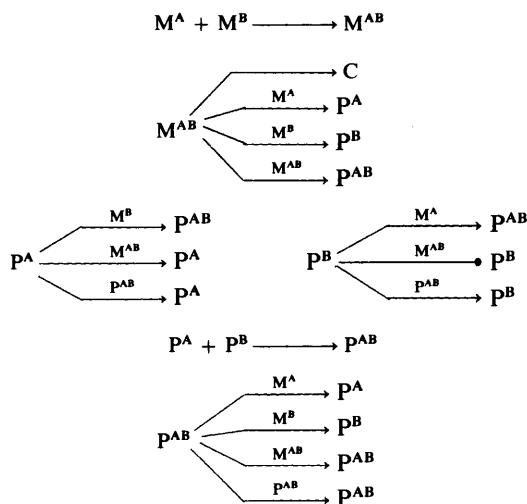
$$d[M^{AB}]/dt' = 4[M^A][M^B] - EM[M^{AB}] - 2[M^{AB}]([M^A] + [M^B] + [M^{AB}] + [P^A] + [P^B]) \quad (9)$$

$$d[C]/dt' = EM[M^{AB}] \quad (10)$$

$$d[P^A]/dt' = 2[M^A][M^{AB}] - 4[P^A]([M^B] + [P^B]) \quad (11)$$

$$d[P^B]/dt' = 2[M^B][M^{AB}] - 4[P^B]([M^A] + [P^A]) \quad (12)$$

The Underestimating Model (UM).—Let us now consider the kinetic model outlined in Scheme 2.



Scheme 2.

In Scheme 2 the polymer p^{AB} is assumed to undergo only intermolecular reactions, which is equivalent to saying that the EMs of the polymeric rings are zero. Neglecting the intramolecular reactions of p^{AB} , Scheme 2 exaggerates the probability of intermolecular reactions between P^{AB} and the other acyclic species, and consequently underestimates the yield of cyclic monomer C.

The set of rate equations relative to the *underestimating*

model, after introduction of the normalizing factor f , can be formulated as follows:

$$d[M^A]/dt' = -2[M^A](2[M^B] + [M^{AB}] + 2[P^B] + [P^{AB}]) \quad (13)$$

$$d[M^B]/dt' = -2[M^B](2[M^A] + [M^{AB}] + 2[P^A] + [P^{AB}]) \quad (14)$$

$$d[M^{AB}]/dt' = 4[M^A][M^B] - EM[M^{AB}] - 2[M^{AB}]([M^A] + [M^B] + [M^{AB}] + [P^A] + [P^B] + [P^{AB}]) \quad (15)$$

$$d[C]/dt' = EM[M^{AB}] \quad (16)$$

$$d[P^A]/dt' = 2[M^A]([M^{AB}] + [P^{AB}]) - 4[P^A]([M^B] + [P^B]) \quad (17)$$

$$d[P^B]/dt' = 2[M^B]([M^{AB}] + [P^{AB}]) - 4[P^B]([M^A] + [P^A]) \quad (18)$$

$$d[P^{AB}]/dt' = 4[M^A][P^B] + 4[M^B][P^A] + [M^{AB}]^2 + 4[P^A][P^B] - [P^{AB}](2[M^A] + 2[M^B] + 2[P^A] + 2[P^B] + [P^{AB}]) \quad (19)$$

The considerations made for the dimerisation of M^{AB} also hold for the dimerisation of P^{AB} .

Batch-wise Procedure.—According to the batch-wise procedure m mol of the monomer M^A and n mol of the monomer M^B are added all at once to a volume V of solvent, where the proper conditions are set. Since higher yields of C are obviously obtained when $m = n$, only this case will be considered. At time $t = 0$ a batch-wise experiment is therefore characterized by the initial concentration $[M^A]_0 = [M^B]_0 = m/V$, the concentration of all other species being zero. By virtue of the equal initial concentrations of M^A and M^B , and of the symmetry of the reacting system, $[M^A] = [M^B]$ and $[P^A] = [P^B]$ over the entire course of the reaction. These equalities considerably simplify the two sets of rate equations (7)–(12) and (13)–(19); in particular equations (8), (12), (14), and (18) become superfluous because they are coincident with equations (7), (11), (13), and (17), respectively. The two reduced sets [equations (7) and (9)–(12) and equations (13), (15)–(17), and (19), respectively] were numerically integrated by the fourth order Runge–Kutta method,⁹ for a number of $[M^A]_0$ and EM values varying over wide ranges, to afford the corresponding values of the final concentration of the cyclic monomer $[C]_\infty$. The percent yield of C, calculated by the equation $\%C = 100[C]_\infty/[M^A]_0$, depends exclusively on the dimensionless parameter α , which is defined by the ratio $[M^A]_0/EM$ and can be viewed as a reduced initial concentration. The results are reported in Figure 1 as plots of $\%C$ vs. α . The two curves which refers to the OM and the UM, interpolate the solutions obtained by numerical integration (*ca.* 50 points for each curve) with a standard deviation $s_{yx} = 0.20$. Both the curves are described by the empirical equation $\%C = 100/(1 + a\alpha^b + c\alpha^d)$ with the following parameters: OM, $a = -2.18$; $b = 1.01$; $c = 4.57$; $d = 0.914$. UM, $a = 8.61 \times 10^{-2}$; $b = 1.50$; $c = 2.98$; $d = 0.804$.

Influxion Procedure.—In the influxion procedure, which corresponds to the well-known Ziegler high-dilution technique,² the monomers M^A and M^B are slowly and simultaneously introduced into the reaction medium in order to prevent their accumulation. An influxion experiment is therefore characterized by the feed rates of M^A and M^B . However, by analogy with the batch-wise experiments, only the case in which the feed rates of M^A and M^B are equal will be considered. The feed rate v_f (in

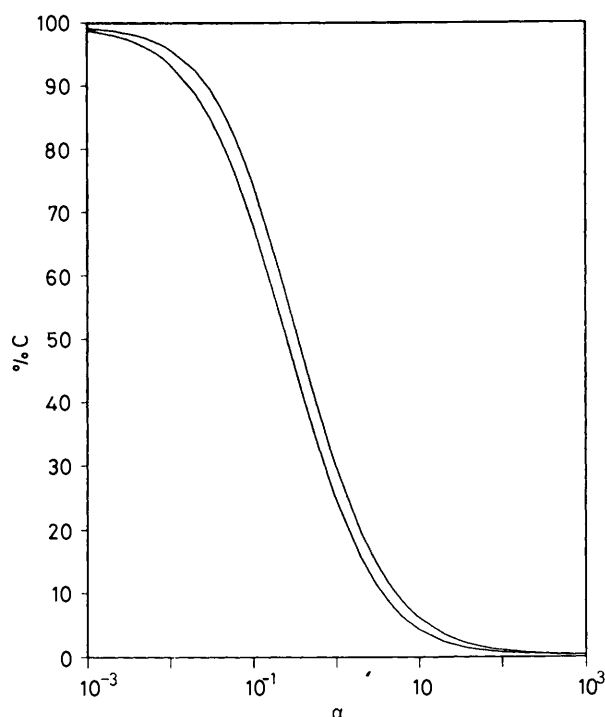


Figure 1. Percentage yield of monomeric ring as a function of α for the A-A + B-B reaction. The upper curve refers to the OM and the lower curve to the UM.

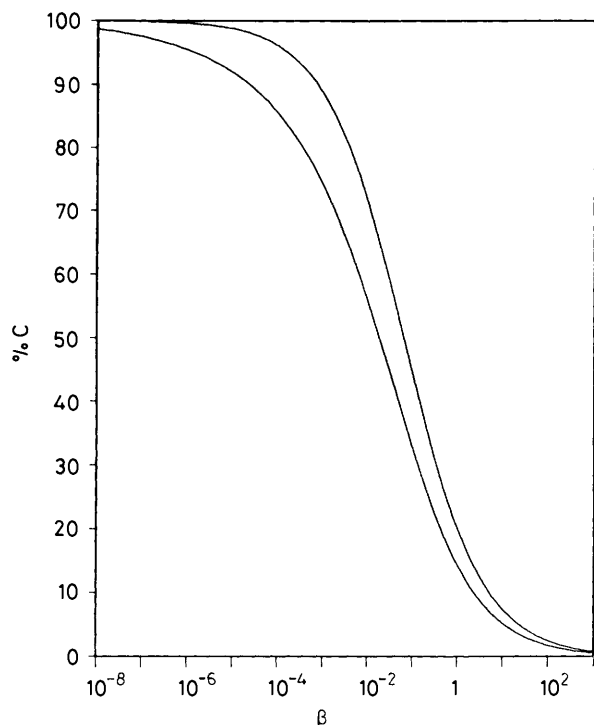


Figure 2. Percentage yield of monomeric ring as a function of β for the A-A + B-B reaction. The upper curve refers to the OM and the lower curve to the UM.

$\text{mol dm}^{-3} \text{ s}^{-1}$) is defined in terms of the number of moles of M^A ($\equiv M^B$) added per second per dm^3 of reaction solution. It is assumed that this addition does not change the volume of the reaction medium to a significant extent.

In order to adapt the two reduced sets of rate equations [(7)

and (9)–(11) and (13), (15)–(17), and (19)] to the influx case, the term v_f ($= v_f/f$) must be added to the left-hand side of equations (7) and (13). Numerical integration of the two systems of rate equations shows that after a certain amount of time a steady state is reached for all of the reacting species. The assumption is made that the steady state is maintained long enough to render negligible the amount of C formed in the initial part (*i.e.* before the steady state is reached) and in the final part (*i.e.* after the addition of reactants is stopped) of the experiment. Therefore, in order to calculate the yield of the cyclic monomer C, one only needs the steady state concentration of M^{AB} ($[M^{AB}]_{st}$). This can be obtained by either the numerical integration procedure or solving numerically the two systems of algebraic equations obtained by setting equal to zero the derivatives of the concentration of the reacting species. The two methods gave coincident results. The percent yield of C calculated by the equation $\%C = 100EM[M^{AB}]_{st}/v_f$, depends exclusively on the dimensionless parameter β , defined as $v_f/k_{inter}EM^2$ ($= v_f/EM^2$). The dependence of $\%C$ on β is shown for the two models in Figure 2. The numerical results (*ca.* 100 points for each model) were interpolated by an equation which has the same form as that relative to the batch-wise case, *i.e.* $\%C = 100/(1 + a\beta^b + c\beta^d)$, with the following parameters: OM, $a = 3.78$; $b = 0.503$; $c = 0.141$; $d = 0.403$ ($s_{yx} = 0.02$). UM, $a = 1.24$; $b = 0.238$; $c = 4.63$; $d = 0.545$ ($s_{yx} = 0.11$).

Discussion

Before discussing the present results it is appropriate to briefly review previous work on the subject.

A computerized game based on Monte Carlo calculations was used by German authors¹⁰ to simulate an influxion procedure in which the formation of cyclic monomer and dimer was taken into account. Apart from the fact that statistical factors for the intermolecular reactions were totally neglected and that the same EM value was attributed to both the cyclic monomer and dimer, a major limitation arises from the fact that the units of the independent variables were not clearly defined, thus making reaction parameters hardly related to actual systems in terms of time, concentrations, feed rate, and the like.

The recent approaches of Fastrez¹¹ and Szwarc,¹² based on the solution of rate equations, are more significant from a quantitative point of view. Fastrez¹¹ considered a number of cases. Some of them, such as the influxion procedure in absence of cyclization or when all of the EMs of the various cyclo-oligomers are identical, are amenable to analytical solution, but cannot be related to actual cases. More significant are the cases (influxion and batch-wise), treated by numerical methods, where the EMs of the various rings are considered to be different. Indeed, extended kinetic schemes taking into account the formation of a number of polymeric rings, such as that proposed by Fastrez for the case A-A + B-B, as well as by us for the case A-B,^{3,5} can afford accurate predictions not only about the yield of the cyclic monomer but also about the yields of the various polymeric rings. However, such extended schemes require knowledge of the EMs of all the rings under consideration. Since, unless the monomeric ring is sufficiently large,* there is no relation between its effective molarity and

* In general, a cycle with $>ca.$ 25 ring atoms can be considered as practically strainless and its EM determined solely by the conformational entropy change upon cyclisation. According to Kuhn's theory,¹³ the effective molarities for cyclisation of a series of chains obeying Gaussian statistics and leading to strainless cyclic n -mers are given by the equation $EM_n = An^{-3/2}$. Note that the effective molarity is denoted in Kuhn's paper by the symbol C_{eff} (effective concentration).

the EMs of the higher cyclo-oligomer, the yield of the cyclic monomer should in principle be represented on a multi-dimensional plot as a function of the various EM values and reaction conditions. This is not, of course, a viable route, and, as a matter of fact, only results pertaining to selected sets of EM values have been reported. Such results, although very useful for illustrating trends in yield distributions of cyclic products, are not of general value.

Similar considerations apply to the work of Szwarc¹² where specific reference was made to the reaction between a living polymer endowed with two reactive end groups and a bifunctional linking agent, which in our language is the case of a A-A + B-B reaction carried out under batch-wise conditions and leading to very large strainless rings.*

Now let us turn to the results reported in this work, considering first those related to the batch-wise technique. As shown in Figure 1, the two kinetic models of Schemes 1 and 2 offer two approximate solutions to the problem of finding the yield of the cyclic monomer for the reaction A-A + B-B. Since the two approximate solutions represent the upper and lower limit for the yield of C, the two curves in Figure 1 delimit a region in which the actual yield of a cyclisation reaction must necessarily lie. This value will be closer to the OM (or to the UM) curve whenever the initial monomer concentration is small (or large) compared to the EM values of the next higher oligomers. In any event, it is remarkable how narrow is the region between the two profiles of Figure 1, which means that even the crudest level of approximation can lead to rather accurate predictions of yields of cyclic monomer, without any assumption being required about the EM values of the polymeric rings.

To profit from the above results, a knowledge of the EM of the monomeric ring is required. In the absence of the required kinetic data, a rough estimate for ring sizes up to *ca.* 25 may be based on the large body of available experimental data,⁸ whereas for larger ring sizes reliable theoretical calculations are possible.^{13,14} On the other hand, Figure 1 itself can provide an estimate for the EM, provided that reliable yield data are available from preliminary experiments. Figure 1 is also useful for pointing out the limitations of the batch-wise procedure. Indeed, if one considers as still acceptable a yield of 50%, it is readily seen that this corresponds to an α value of *ca.* 0.3, which means that rings with EMs $< 0.03 \text{ mol dm}^{-3}$ cannot be synthesised in reasonably high yield in batch processes, because reactant concentrations $< 1 \times 10^{-2} \text{ mol dm}^{-3}$, *i.e.* too low for most practical purposes, should be used. This indicates that the batch-wise procedure can be still conveniently employed for the synthesis of large, strainless rings whose EMs lie almost invariably in the range 0.1–0.01 mol dm^{-3} , with a definite tendency to cluster in the region of 0.03 mol dm^{-3} .⁸ But in the case of the strained medium rings, for which typical EMs are in the range of 10^{-3} – $10^{-5} \text{ mol dm}^{-3}$, or even lower,⁸ the fate of a batch process is to afford a few percent yield of the desired ring, if any.

Let us now consider the influxion case. Here again we see that the curves corresponding to the two models (Figure 2) delimit a region where the actual yield will necessarily lie. This value will be more or less proximate to either curve, depending on the relative value of the steady concentration of monomers with respect to the EM values of the next higher oligomers. We note, however, that the region between the two curves turns out to be much wider than that found for the batch-wise case (Figure 1). In spite of the lower predictive power of Figure 2, the general behaviour of the curves allows some interesting features to be delineated.

The preparative usefulness of the influxion technique, as compared to the batch-wise one, is largely dependent on the value of k_{inter} . In fact, the significant amount of solvent saved

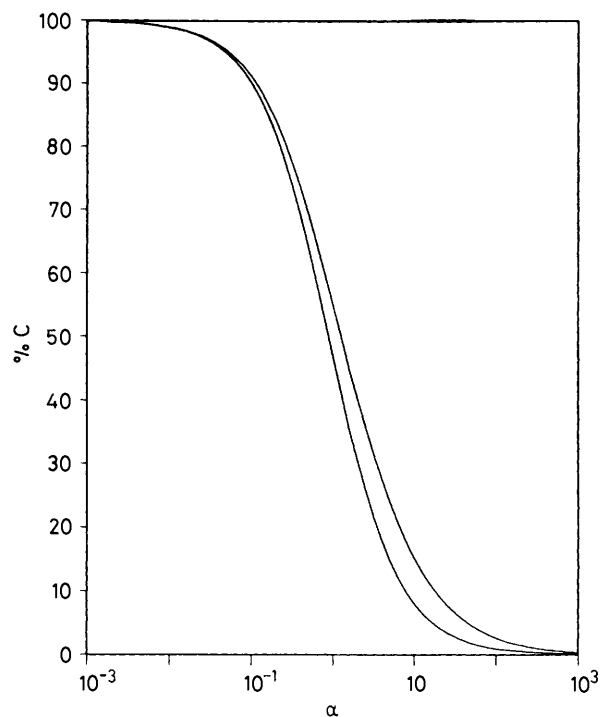


Figure 3. Percentage yield of monomeric ring as a function of α for the A-B reaction. The upper curve refers to the OM and the lower curve to the UM.

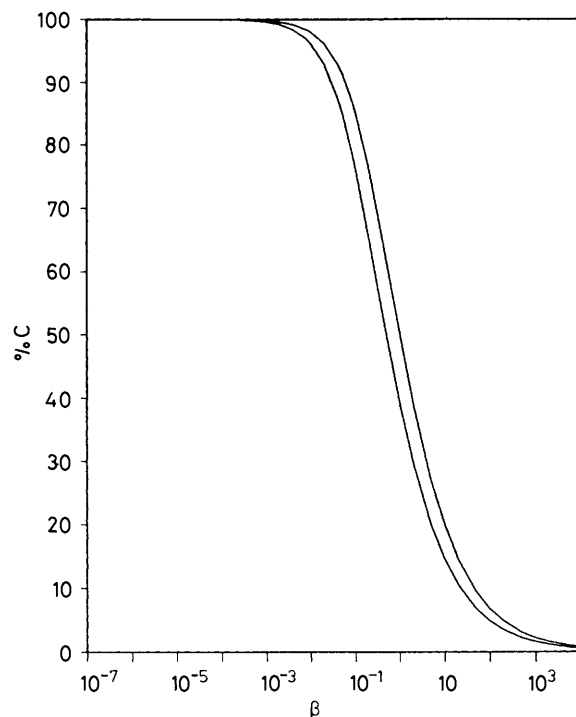


Figure 4. Percentage yield of monomeric ring as a function of β for the A-B reaction. The upper curve refers to the OM and the lower curve to the UM.

in an influxion experiment *vs.* the amount required in the corresponding batch process, must be necessarily paid with a more prolonged reaction time. It emerges from the definition of

* See footnote on p. 749.

β that in order to reduce this time to a minimum, k_{inter} should be as large as possible. One should also note that an inherently faster reaction will give, other things being equal, a higher yield of cyclic monomer. A numerical example illustrates well the above points. If we want a given two-component ring closure reaction to afford the desired monomeric ring in yield not $< 50\%$, the parameter β , as estimated from Figure 2, should be not $> ca. 4 \times 10^{-2}$. Since feed rates $< 1 \times 10^{-6} \text{ mol dm}^{-3} \text{ s}^{-1}$ (corresponding, e.g., to the addition of 0.1 mol of M^A and M^B to 1 dm^3 of solvent in ca. 28 h) are obviously undesirable, it is easily seen that monomeric rings with $EM < 5 \times 10^{-3} \text{ mol dm}^{-3}$ are hardly accessible by reaction of two symmetrical monomers if the inherent reactivity of functional groups k_{inter} is $< 1 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. In fact, a five-fold lower EM would require a 25-fold lower feed rate, which corresponds in the given example to a total addition time of ca. 1 month. It is clear that with highly disfavoured rings the only viable route is to increase the inherent reactivity of end groups as much as possible. This can be accomplished by the resourceful use of all available principles and rules governing the activation of reacting groups.

One-component vs. Two-component Ring Closure.—It is of interest to compare the results from the present work with analogous results previously reported for the one-component ring closure of unsymmetrical bifunctional chains A–B.^{3,5} These are plotted in Figures 3 and 4 for the batch-wise and influxion procedure, respectively.* Yield profiles as a function of the parameters α and β were calculated on the basis of both the UM and OM at the lowest level of approximation, which renders the results for closure of A–B chains strictly comparable to those related to the two-component ring closure A–A + B–B. Inspection of Figure 1 vs. Figure 3, and of Figure 2 vs. Figure 4 shows that the general dependence of yields on the dilution parameters α and β is broadly similar in the two cases, but there are important differences. The profiles for the two-component ring closure are somewhat shifted towards lower α and β values relative to the one-component system. For example, the percent yields predicted when $\alpha = 1$ by the UM and OM for the one-component cyclisation under batch-wise conditions are 46.7 and 54.9, respectively (Figure 3), but the corresponding figures drop to 24.7 and 29.8 (Figure 1) for the two-component cyclisation. Differences are even more marked for the influxion case in that when $\beta = 1$ the yields are 44.2 and 50 for the one component cyclisation (Figure 4), but reduce to 14.5 and 20.3 for the two component reaction (Figure 2). Thus the obvious advantage of working with more readily accessible symmetrical reactants is offset by more stringent dilution requirements. It therefore appears that, other things being equal, rings which are difficult to form should be more easily synthesised by one-component ring closure reactions, particularly when the influxion technique is the procedure of choice.

Merging of Influxion into Batch-wise Conditions.—Our calculations have been based on the assumption that in influxion experiments the steady state is maintained long enough so as to render negligible the amounts of product

* The curve in Figure 3 which interpolates the numerical solutions of the UM batch-wise is described by the empirical equation $\%C = 100/(1 + a\alpha^b + c\alpha^d)$ with the following parameters: $a = -1.55 \times 10^{-2}$; $b = 1.61$; $c = 1.15$; $d = 1.02$ ($s_{yx} = 0.21$). Although in our previous work³ a different fitting equation was suggested, we prefer this one because it has the same form as those reported in this work. As for the other curves reported in Figures 3 and 4, they refer to analytical solutions.^{3,5}

† It can be shown that strictly analogous conclusions are reached using the UM set.

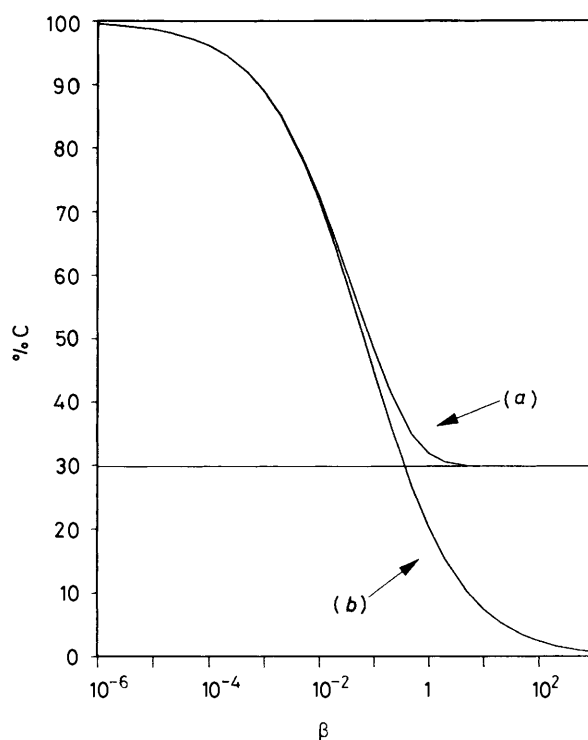


Figure 5. Merging of influxion into batch-wise conditions (see the text).

formed before the steady state is reached and after the addition of reactants is stopped. Indeed this assumption raises two principal questions: (i) In actual experiments is the steady state reached at all? (ii) If it is reached, how can one be sure that it will last long enough? In order to answer the above questions, a numerical example is appropriate. Let us suppose that the starting materials to submit to influxion are 10 mmol of M^A and M^B , the volume of the reaction medium is 1 dm^3 , the EM of the cyclic monomer, 0.01 mol dm^{-3} ; and k_{inter} , 1 $\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$. With these data let us calculate the yield of C as a function of the feed rate by numerically integrating the OM set† of rate equations up to completion of the reaction, no matter whether the steady state is reached or not. The results are plotted against β in Figure 5 [curve (a)]. For comparative purposes the upper curve of Figure 2 has been reproduced in Figure 5 [curve (b)]. It appears that curve (a) is always higher than that calculated by the steady state assumption, the difference between the two curves becoming smaller as the feed rate decreases. In general, whenever the feed rate increases, the influxion procedure approaches the batch-wise procedure, in that curve (a) tends to a limiting value of the yield which is exactly that corresponding to the instantaneous addition of M^A and M^B into the reaction medium. Since such addition, in the given example, corresponds to $\alpha = 1$, the limiting value of the yield (29.8%) coincides with that calculated from the upper curve of Figure 1. The horizontal line corresponding to $\%C = 29.8$ intersects curve (b) at a value of β which is critical (β_{cr}), i.e. when $\beta > \beta_{\text{cr}}$, those values which were intended to be influxion conditions turn out to be batch-wise conditions (or very nearly so), whereas when $\beta < \beta_{\text{cr}}$, curve (a) is satisfactorily approximated by curve (b) which describes the influxion behaviour. In conclusion, to profit from the results of Figure 2, one does not need to worry about the fulfilment of the steady state assumption, but should bear in mind that Figure 2 is significant only for $\beta < \beta_{\text{cr}}$. The value of β_{cr} can be evaluated for any particular reaction system as follows: (i) calculate the value of α corresponding to the instantaneous addition of the monomers; (ii) evaluate by means of Figure 1 the $\%C$ value ($\%C_{b-w}$) as given by one of the two

models corresponding to the calculated α value; and (iii) evaluate the β value (β_{cr}) corresponding to $\%C_{b-w}$, by using the curve in Figure 2 which refers to the same model. Although β_{cr} evaluated by the two models is not exactly the same, it should be clear, as Figure 3 shows, that β_{cr} is not a point of discontinuity but rather the approximate centre of a region in which the influxion procedure merges into the batch-wise one. Of course, strictly analogous considerations hold for the one-component ring closure as well.

When an influxion experiment is carried out in the absence of any information about the quantities EM and k_{inter} , which is likely to be most often the case, it may well happen that the various parameters combine in such a way that the system is actually described by a point in the flat portion of curve (a) (Figure 5). When this is the case, the system can seemingly display an intriguing insensitivity to dilution, which might well mislead the experimenter to postulate the operation of special effects, such as template effects, and the like.

Conclusions

In spite of the inherent complexity of systems in which polymerisation significantly competes with cyclisation, approximate kinetic models, amenable to numerical solution, predict in a satisfactory manner yields of ring products that can be obtained under a given set of experimental conditions. The advantage of the proposed models is that maximum-error estimates of the calculated yields are immediately available by comparing results from the UM with those from the OM. Besides providing a background for the correct interpretation of cyclisation experiments, the results can supply the synthetic chemist with useful guidelines for the search of optimum reaction conditions, in terms of the concentration of reactants in batch processes, or in terms of rate of feed in influxion experiments.

More or less marked deviations from the yield range whose boundaries are predicted by the two models are to be expected in a number of cases, *i.e.* when: (i) the requisite of independent reactivity of the terminal groups is not satisfied; (ii) the reaction medium is not homogeneous; (iii) side-reactions occur; (iv) the

reaction is not carried out to completion; and (v) a yield-enhancing effect operates.

It should be clear that the latter case should manifest itself by experimental yields of monomeric rings lying significantly above the curve of the OM. This would be good evidence with which to sustain the validity of yield-enhancing effects which have been claimed to operate in certain macrocycle syntheses,^{2,15} such as the caesium effect, hydrophobic coiling, the rigid group principle, the *gauche* effect, as well as some of the template effects.

References

- 1 Part 28 of the series 'Ring-Closure Reactions,' Part 27, ref. 5.
- 2 L. Rossa and F. Vögtle, *Top. Curr. Chem.*, 1983, **113**, 1.
- 3 G. Ercolani, L. Mandolini, and P. Mencarelli, *Macromolecules*, 1988, **21**, 1241.
- 4 G. Ercolani and P. Mencarelli, *J. Chem. Soc., Perkin Trans. 2*, 1989, 187.
- 5 G. Ercolani, L. Mandolini, and P. Mencarelli, *Gazz. Chim. Ital.*, 1989, **119**, 209.
- 6 P. J. Flory, *Chem. Rev.*, 1949, **39**, 137.
- 7 A. Kirby, *Adv. Phys. Org. Chem.*, 1980, **17**, 183.
- 8 L. Mandolini, *Adv. Phys. Org. Chem.*, 1986, **22**, 1.
- 9 H. Margenau and G. M. Murphy, 'The Mathematics of Physics and Chemistry,' D. van Nostrand Company, Princeton, 1962, pp. 486-487.
- 10 E. Hammerschmidt, H. Schutter, and F. Vögtle, *J. Chem. Res.*, 1980 (S), 86; (M), 1083.
- 11 J. Fastrez, *Tetrahedron Lett.*, 1987, **28**, 419; *J. Phys. Chem.*, 1989, **93**, 2635.
- 12 M. Szwarc, *Makromol. Chem.*, 1989, **190**, 567.
- 13 W. Khun, *Kolloidn. Zh.*, 1934, **68**, 2; H. Morawetz 'Macromolecules in Solution,' Wiley, New York, 1975, pp. 439-488.
- 14 P. J. Flory, U. W. Suter, and M. Mutter, *J. Am. Chem. Soc.*, 1976, **98**, 5733, 5740, 5745.
- 15 X.-K. Jiang, Y.-Z. Hui, and Z.-X. Fei, *J. Chem. Soc., Chem. Commun.*, 1988, 689.

Paper 9/03452H

Received 11th August 1989

Accepted 31st October 1989